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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/699,818	10/30/2000	Brian L. Ganz		7165

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John R Ross III
Ross Patent Law Office
P O Box 2138
Del Mar, CA 92014

EXAMINER

GORDON, BRIAN R

ART UNIT PAPER NUMBER

1743

DATE MAILED: 06/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/699,818

Applicant(s)

GANZ ET AL.

Examiner

Brian R. Gordon

Art Unit

1743

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM
THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-41 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-19 and 21-41 is/are rejected.
- 7) ☒ Claim(s) 20 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 12, 2004 has been entered.

Response to Arguments

2. Applicant's arguments, see remarks, filed March 12, 2004, with respect to Marouiss being an improper reference have been fully considered and are persuasive. The previous 103 rejections of claims 1-41 based on Marouiss have been withdrawn.

Claim Interpretations

As to claims 7-15 and 19, the examiner hereby submits that the claims are not structural limitations of the device but are moreso directed to the capability of the device and the data transmitted from the camera to the computer.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 36 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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5. Claim 36 recites the limitation "said walking bean indexer" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-19, 21-22, 25-27, and 29-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stylli et al. US 6,685,884 further in view of Roberts et al. US 5,871,696.

Stylli et al. disclose a high throughput chemical screening method uses methods of concurrent transport and/or processing to increase throughput. A screener may concurrently retrieve chemicals from an addressable chemical storage module and deliver chemicals to a liquid handling module. The screener may also use one transport lane for moving chemicals away from a storage module, and a second transport lane for moving chemicals toward the storage module.

Such a system, as shown in FIG. 1, usually includes the following components: a) a storage and retrieval module for storing and retrieving very large numbers (at least about 100,000) of different reagents in containers, b) a sample distribution module to handle (e.g., aspirate samples from containers (sample removal area) and dispense samples (dispense head) into sample containers) small volumes of liquids at a high rate of speed, c) a sample transporter (microplate indexing device) to transport reagents from a selected component to another at a compatible throughput rate, d) a reaction module (e.g., a reagent dispenser or a detector) for chemical reactions or physical measurements at high throughput rates, and e) a data processing and integration module that can control module operation.

The modules can be separately controlled or programmably controlled and integrated using a data processing and integration module. The data processing and integration module permits orchestrated processing to deliver addressable chemical

wells or addressable sample wells to workstations so as to reduce processing time and permit, if so desired, parallel processing of addressable chemical wells or addressable sample wells. Typically, the storage and retrieval module, sample distribution module, sample transporter, reaction module and data processing and integration module are operably linked to facilitate rapid processing of the addressable sample wells or the addressable chemical wells.

The invention provides for a sample distribution module that can dispense or aspirate large numbers of solutions, usually small volume solutions. The sample distribution module will often include a plate buffer (e.g., a stacker). The random access high density plate presentation module comprises a plurality of stacks, preferably removable stacks, that hold plates. Each stack is connected to either a platen or a conveyor system that has a lifting platen that either stacks or destacks plates by engaging the plate bottom. When the sample distribution module is integrated with a storage and retrieval module, it will be advantageous for the sample distribution module to both aspirate and dispense solutions with a liquid handler. In many instances, the sample distribution module will hold large numbers of different stock solutions of chemicals dissolved in aqueous or non-aqueous solvents (e.g., water or dimethylsulfoxide (DMSO)) in addressable chemical wells. To facilitate the rapid transfer of these stock solutions, it is desirable for the sample distribution module to aspirate a stock solution from an addressable well and dispense all or a portion of that solution into an addressable sample well or another addressable well. This sequence of events can be programmably controlled to ensure that the stock solution is aspirated from a pre-

selected addressable chemical well and is dispensed into a pre-selected addressable sample well. This type of sample distribution module and process is useful for generating daughter plates from master plates or for transferring and diluting a chemical solution from a chemical plate to a sample plate. Typically, a sample transporter can be used to mechanically link the sample distribution module to a storage and retrieval module for the preparation of daughter plates. The sample distribution module can also be integrated to other components, for instance a conveyor transport system can link a sample distribution module to a reaction module.

Nanoliter dispensers comprise an electrically sensitive volume displacement unit in fluid communication to a fluid reservoir. Typically, the fluid reservoir holds liquid aspirated from an addressable chemical well. Electrically sensitive volume displacement units are comprised of materials that respond to an electrical current by changing volume. Typically, such materials can be **piezo** materials suitably configured to respond to an electric current. The electrically sensitive volume displacement unit is in vibrational communication with a dispensing nozzle so that vibration ejects a predetermined volume from the nozzle. Preferably, piezo materials are used in dispensers for volumes less than about 10 to 1 nanoliter, and are capable of dispensing minimal volumes of 500 to 1 picoliter. Piezo dispensers can be obtained from Packard Instrument Company, Conn., USA (e.g., an accessory for the MultiProbe 104). Such devices can also be used in other liquid handling components described herein depending on the application. Such small dispensation volumes permit greater dilution, conserve and reduce liquid handling times.

Fluorescence in a sample can be measured using a detector described herein or known in the art for multi-well plates. In general, excitation radiation, from an excitation source having a first wavelength, passes through excitation optics. The excitation optics cause the excitation radiation to excite the sample. In response, fluorescent probes in the sample emit radiation which has a wavelength that is different from the excitation wavelength. Collection optics then collect the emission from the sample. The device can include a temperature controller to maintain the sample at a specific temperature while it is being scanned. According to one embodiment, a multi-axis translation stage (e.g., a dedicated X, Y positioner) moves a microtiter plate holding a plurality of samples in order to position different wells to be exposed. The multi-axis translation stage, temperature controller, auto-focusing feature, and electronics associated with imaging (camera) and data collection can be managed by an appropriately programmed digital computer. The computer also can transform the data collected during the assay into another format for presentation.

The plates in the system are labeled with bar codes. When used with a data processing and integration module controller, the bar code can easily reference a plurality of plate and well information from the data store, such that no encoded data is necessary on the bar code itself. In one embodiment, the screening sample distribution module was designed with a **bar code reader** to scan incoming plates and verify plate location in the screening sample distribution module and to permit location of an addressable well. Typically, bar codes are detected to locate plates before any manipulation is performed.

Performance of a function outside of measurable parameters will also constitute an error. Errors will be corrected automatically (adjustment means) when within the ability of the instrument to do so. Unrecoverable errors can notify the user via both the touch screen and the external link, and will set the handshaking logic to refuse further plate input, until the error is corrected. For given families of error conditions, a response can be specified, e.g., for recoverable errors, bar code errors. For errors that are automatically recoverable, response parameters will exist to either pause the instrument and report the error, or to automatically recover from the error, report/log the error and resume operation. Recoverable errors will have a time-out function to halt recovery, if time exceeds a configurable value.

In one embodiment, the screening sample distribution module was designed with a bi-directional plate delidder and relidder. The lidder removes and replaces plate lids at a rate of about 5 to 11 plates per minute in one direction. The lidder can store approximately 60 lids. Preferably, a modified lid is used for separation.

Stylli et al. does not disclose that the target location for dispensing the samples are slides.

Roberts et al. disclose a cassette for blood smear slides has a holder portion for supporting slides in a stack and an alignment surface for orienting a bottom slide with respect to a slide egress window. A force plate member is urged against the top slide in the stack with a constant force spring to align the bottom slide and to retain the slide stack.

The cassette provides for consistency in feeding single slides into a precise orientation for pickup by a slide manipulation assembly of an automated blood smear slide making apparatus.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Stylli et al. to incorporate the slide cassette of Roberts et al. al to allow for the analysis or detection of target components in a small amount of blood samples numbering less than the number of wells in a plate to maximize the efficiency of operation of the device.

10. Claims 23 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stylli et al. in veiw of Roberts et al. as applied to claims 1-19, 21-22, 25-27, 29-35, and 37 above, and further in view of Palcic et al. US 6,026,174.

Stylli et al. do not disclose that the substrate is a slide or that the device further comprises a CCD camera

Palcic et al. US 6,026,174 discloses a system and method for automatically detecting diagnostic cells and cells having malignancy-associated changes (MAC).

The MAC detection system according to the present invention is shown in FIG. 1. The system 10 includes a digital microscope 12 that is controlled by and interfaced with a computer system 30. The microscope 12 preferably has a digital CCD camera 14 employing a scientific CCD having square pixels of approximately 0.3 mm by 0.3 mm size. The scientific CCD has a 100% fill factor and at least a 256 gray level resolution. The CCD camera is preferably mounted in the primary image plane of a planar objective lens 22 of the microscope 12. A stable light source 18, preferably with

feedback control, illuminates the cell sample while an image of the slide is being captured by the CCD camera. The lens 22 placed between the sample 16 and the CCD camera 14 is preferably a 2x/0.75 objective that provides a depth of field in the range of 1-2 mm that yields a distortion-free image.

The images produced by the CCD camera are received by an image processing board 32 that serves as the interface between the digital camera 14 and the computer system 30. The digital images are stored in the image processing board and manipulated to facilitate the detection of MACs. The image processing board creates a set of analog video signals from the digital image and feeds the video signals to an image monitor 36 in order to display an image of the objects viewed by the microscope.

An image of a frame from the slide is captured by the CCD camera and is transferred into the image processor. In this process, the CCD sensor within the camera cleared and a shutter of the camera is opened for a fixed period that is dependent on the intensity of the light source 18. After the image is optimized according to the steps described below, the stage then moves to a new position on the slide such that another image of the new frame can be captured by the camera and transferred into the computer memory. Because the cell sample on the slide occupies a much greater area than the area viewed by the microscope, a number of slide images are used to determine whether the sample is MAC-positive or negative. The position of each captured image on the slide is recorded in the computer system so that the objects of interest in the image can be found on the slide if desired.

Once an image from the slide is captured by the CCD camera and stored in the image processing board, the computer system determines whether the image produced by the CCD camera is devoid of objects. This is performed by scanning the digital image for dark pixels. If the number of dark pixels, i.e., those pixels having an intensity of the background intensity minus a predetermined offset value, is fewer than a predetermined minimum, the computer system assumes that the image is blank and the microscope stage is moved to a new position at step 60 and a new image is captured at step 54.

It would have been obvious to one of ordinary skill in the art to modify the modified the modified device of Stylli. It would have also been obvious to use the camera of Little as and using the CCD camera present as an additional form or means of analysis (additional to e.g., spectrometric techniques, such as UV/IVIS, IR, fluorescence, chemiluminescence, NMR spectroscopy or mass spectrometry) for the samples deposited on the substrate.

As to claim 24, it would have also been obvious to provide the array on a vibration isolated base when one is attempting to dispense a precise volume of fluid when required.

11. Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stylli et al. in view of Roberts et al. as applied to claim claims 1-19, 22, 25-27, 29-35, and 37 above, and further in view of Overbeck.

Stylli et al. in view of Roberts et al. does not disclose the use of quill type dispensers.

Overbeck discloses a fluid deposit assembly in which piezo and quill type dispensers are used to jet small volumes of fluid to a substrate.

It would have been obvious to one of the ordinary skill in the art at the time of the invention to modify the modified device of Stylli by employing the teachings of Overbeck for quill and piezo dispensers are capable of depositing very small volumes of fluid as well as the employment of quill tips allows one to suck up a desired amount of fluid (column 2 lines 8-18).

Allowable Subject Matter

12. Claim 20 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

13. The following is a statement of reasons for the indication of allowable subject matter: The prior art does not teach nor fairly suggest microarrayer further comprising at least one cleaning station, comprising: A) a sonic cleaner, B) a rinsing fountain, and C) a vacuum manifold.

Conclusion

14. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.


Taylor et al., Pfost et al. Guirguis , and Cousino et al. disclose slide processing devices.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian R. Gordon whose telephone number is 571-272-1258. The examiner can normally be reached on M-F, with 2nd and 4th F off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

brg


Jill Warden
Supervisory Patent Examiner
Technology Center 1700